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Research paper

Retrospective observational study and comparative review of lymph node yield in open vs. laparoscopic surgery for colorectal cancer

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Abstract

Laparoscopic surgery is standard treatment for colorectal cancer in the last decade of surgery's history. Nowadays open surgery for CRC indicated only for certain cases. with evolving of laparoscopic instruments and adoption of laparoscopic and robotic techniques by new generation of surgeons open surgery started to vanish gradually as standard care in all world well equipped hospitals and centers . Short and long term advantages of laparoscopic approach manifested in it is minimum invasive technique and less sequelae of wound healing respectively, but in CRC surgical procedures staging and eradication of neoplasm have great impact in survival and morbidity outcome. This study compare laparoscopic with open surgical technique for CRC using lymph node yield as oncological determinant factor for prognosis and need for further treatment.

Keywords: *Laparoscopic CRC surgery, open CRC surgery, lymph node yield and oncological relevance.*

1. Introduction

Laparoscopic surgery has gained increasing popularity for treatment of colorectal cancer. According to the American Board of colorectal surgery, already in 2005, about 24.3% of laparoscopic colorectal surgery was performed for oncologic indications. In the same year, about 41.1% of surgical operations for colorectal cancer were accomplished laparoscopically . Nowadays, the trend towards laparoscopic technique in colorectal surgery, either for benign or malignant disease, is continuously rising up. open technique in colorectal cancer surgery as care diminished gradually in favour of minimal invasive surgery , laparoscopic and robotic CRC resection approved to be with better outcome than open surgery in morbidity , recovery , length of hospital stay and complications , despite this advantages still questionable whether lymph node yielding is different between open and laparoscopic technique.

One of the mainstay prognostic indicator is involvement of lymph node, this will govern the need for adjuvant or neoadjuvant chemotherapy and give drastic prognosis in natural history of CRC.

Patients with negative lymph node in CRC have 70 % to 80 % 5 year survival rate while with lymph node metastasis have only 30% to 60 %. In this study I compared the lymph node yield between open and laparoscopic technique using 12 lymph nodes as standard for oncological resection.

Number of lymph node harvested in colorectal surgery considered crucial and have great impact in treatment, survival and prognosis . yielding of lymph nodes can be affected by multifactor like surgical technique , histopathologist , location of the tumour and many other factors , in this study we tried to search if there is any difference between open and laparoscopic technique using review of more than 20 published studies ,

Lymph node drainage system of large bowel have the same complexity as it is blood supply and interlinked with circuit of lymph channels , so the lymphatic drainage of large bowel conveyed in the mesentery and regionally distributed as blood supply , skip lesion can happen either for anatomical variant or congenital anomalies.

In study published 2019 Orsenigo E, et al. in Italy , Milano involved 2319 patients and it is multisystematic review showed there is different factors in addition to anatomical variant and anomalies influence lymph node yielding and retrieval , this factor subjected to uni- and multivariate analyses. Moreover, a survival analysis was carried out to verify the prognostic implications of nodal counts. The mean number of evaluated nodes was 24.08 ± 11.4, 20.34 ± 11.8, and 15.33 ± 9.64 in surgically treated right-sided colon cancer, left-sided colon cancer, and rectal tumours, respectively. More than 12 lymph nodes were reported in surgical specimens in 1094 (86.9%) cases in the colon cohort and in 425 (63%) cases in the rectal cohort, and patients who underwent neoadjuvant chemoradiation were analysed separately. On univariate analysis of the colon cancer group, higher LNs counts were associated with female sex, right colon cancer, emergency surgery, pT3-T4 diseases, higher tumour size, and resected specimen length (1).

Adopted practise recommend yielding of at least 12 lymph nodes in colonic cancer resection, number of lymph node harvested will be a challenge for surgical technique in addition to histopathologist and patient factor.

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Aim of the study
The aim of this study is to compare the lymph node yield between open and laparoscopic technique using 12 lymph node as standard for oncological resection.

2. Literature review

In both laparoscopy and open technique high ligation of pedicles is debatable as independent factor whether of oncological benefit or not , in systematic review and meta analysis study Si MB, et al. Published June 2019 In total, 30 studies were included in this analysis. There were significantly higher odds of anastomotic leakage and urethral dysfunction in patients treated with high ligation compared to those treated with low ligation (OR = 1.29; 95% CI = 1.08 to 1.55; OR = 2.45; 95% CI = 1.39 to 4.33, respectively). There were no significant differences between the groups in terms of the total number of harvested lymph nodes, the number of harvested lymph nodes around root of the IMA, local recurrence rate, and operation time. Further, no statistically significant group differences in 5-year overall survival rates and 5-year disease-free survival rates were detected among all patients nor among subgroups of stage II patients and stage III patients, respectively. Concluded low ligation can achieve equivalent lymph node yield to high ligation, and both procedures have similar survival benefits. However, low ligation is associated with a lower incidence of leakage and urethral dysfunction. Thus, low ligation is recommended for colorectal cancer surgery(2).
In contrast to level of pedicle ligation as technique to harvest lymph node , lymph node number harvested it self act as mean survival factor , this had been approved in multiple studies and standard practise of today ; recent study August 2019 (Annals of surgery)Trepanier M, et al conducted systemic review of 261,423 patients were included. Restricted cubic splines demonstrated that the adjusted improvements in overall survival stabilized after 24 nodes. Patients were divided into: <12, 12 to 23, and ≥24 nodes. On survival analysis, patients with ≥24 nodes had better survival across all N stages compared to other groups (P < .001). Lymph node harvest ≥24 nodes was independently associated with improved overall survival compared to 12 to 23 nodes (hazard ratio 0.82; 95% confidence interval, 0.80-0.85) , concluded that Lymph node harvest ≥24 nodes is associated with improved survival in colorectal cancer patients(3).
In Italian study Giovanni Ramacciato et al. Chir Ital. Jan-Feb 2008 it favour open resection for number of lymph node harvested in Right hemicolectomy against laparoscopic assisted Right hemicolectomy , In the LRH group a median of 12.7 lymph nodes were removed (range: 9-31; SD +/- 4.5) vs. 18 lymph nodes in the ORH group (range: 8-29; SD +/- 3.9) ($p < 0.05$). Associated surgery was performed in 15.1% of cases in both groups. In this study LRH presents a statistically significant advantage in terms of morbidity and blood loss compared to ORH. Equivalent oncological clearance was obtained, fulfilling the stated criteria of 5 cm free resection margins and number of lymph nodes resected, though we removed fewer lymph nodes in LRH compared to ORH ($p < 0.05$). but more recent randomized control study published in American Journal of Surgery 2017 JeffreyDouaihera Sean JLangenfeldce l showed significant oncological benefit of lymph node Number harvested with laparoscopy comparing with open technique Retrospective study using the colectomy-targeted American College of Surgeons National Surgical Quality Improvement Program for years 2014–2016. Primary outcome was resection of at least 12 nodes. Univariate and multivariate analyses determined factors associated with ≥12 LN yield. Result for colon cancer were extracted from the NSQIP database. 7.26% of cases did not reach a 12 LN harvest.
Harvesting ≥12 LN was 74% more likely ($p = 0.001$) if the resection was laparoscopic and 72% more likely ($p < 0.0001$) if hand-assisted. Advanced T and N stage had a higher likelihood of reaching 12 LN harvest.
Older age, female gender and smoking history decreased the likelihood of ≥12 LN harvested, conclusion Laparoscopic and robotic colectomies were 1.5–2.5 times more likely to achieve adequate LN harvest compared to open surgery. Several non-modifiable patient and disease related factors may render adequate LN yield challenging. Testing the difference of lymph node yielding between open vs laparoscopic technique it will affect the practise even so the prevalence of minimally invasive surgery.
Further more recent randomized control study in Taiwan June 2019, 375 colorectal cancer patients under Dr. Chiu's service were sorted. Of these, 11 were excluded from the study. A total of 364 patients receiving curative resection were assessed in this study; 195 received LR and 169 received OR.
Carcinomatosis was detected intra-operatively in seven patients of LR and six patients of OR, which were excluded. The remaining patients were compliant with the follow-up protocol. The median surveillance period was about 60 month , both groups of patients were well matched in terms of demographic and clinicopathologic parameters. During this study period, 188 patients of the LR group were compared with the data obtained from the other 163 patients of the OR group. In the LR group, the mean age was 68.6 ± 12.7 years, and 102 (54.3%) patients were male. According to the final pathology report, three patients were classified in stage 0, 68 in stage I, 30 in stage II, and 87 in stage III. In the OR group, the mean age was 71.5 ± 12.1 years, and 87 (53.4%) patients were male; none were affected by tumours in stage 0, 53 in stage I, 29 in stage II, and 81 in stage III. There was a little disparity between clinical/radiologic staging and pathological staging in this study. Other characteristics of tumours and patients were summarized, and there was no statistical difference between these two groups. Surgical.
Outcomes showed the rate of tumour recurrence was 9.0% (17/188) in the LR group and 13.5% (22/163) in the OR group. Although the difference was not statistically significant, tumour recurrence seemed to be lower in the LR group ($p = 0.186$). The average number of lymph nodes removed in LR was 16.0 ± 9.2 and 19.2 ± 13.7 in OR ($p = 0.07$). Tumour margins were non-involved in patients of both groups. However, this study demonstrated that LR was more effective for the treatment of colorectal cancer in terms of hospital stay ($p < 0.001$) and blood loss ($p < 0.001$). Conversely, operation time was significantly longer in LR than in OR (191.4 ± 71.1 min vs. 150.8 ± 46.3 min, $p < 0.001$). Compared with the LR group, more patients in the OR group encountered postoperative urinary tract infection, wound infection, and pneumonia, which reached statistical significance. Only two patients in the OR group were found with mild anastomosis leakage from the drainage tube clinically. Abdominal CT confirmed the diagnosis and that the degree was mild. These two patients received conservative treatment, including intravenous fluid supply and nil per mouth. However, further surgical intervention was not necessary.
The review showed Laparoscopic technique have better oncological outcome regarding Number of lymph nodes harvested in addition to benefit of short hospital stay , less morbidity , less need for blood transfusion , less postoperative stress and less recurrence rate. Still few studies showing no oncological significant differences and pitfall of cost when comparing laparoscopy with open technique.

3. Materials & methods

The research design used was a retrospective cohort observational study involving CRC histology samples plotted with technique of surgery from 2012 to 2016 in Limerick university hospital.

I collected colorectal data when I started my Master in NUI in 2016 from Limerick university hospital where I was senior surgical registrar in that hospital. I collected over 100 histology reports for colorectal cancer cases since 2012 in order to compare the lymph node yield with operative technique (open vs laparoscopic), my data collection was widened to involve aggressive histological features including: lymphovascular, perineual invasions and satellite lesion.

4. Results

The total number of CRC operated cases during the study period (2012 and 2016) was 152; of which 28 were open and 124 were Laparoscopic (Table 1).

Table 1: Total Number of Samples

Laparoscopic (UHL cases done 2012 to 2016)	Open (UHL cases done 2012 to 2016)
124	28

The data showed the highest yield was 39 lymph nodes reported in laparoscopic technique while the highest yield in open technique only 31. The lowest yield was 0 lymph node which was reported in both techniques (table2)

Table 2: Lymph Node Yield in both Technique with Total Number of Positive and Negative Lymph Node

Lymphnodes yield in laparoscopic cases	Lymphnodes yield in open cases	
1-15/2		
2- 14/0		
3- 34/4		
4- 18/3		
5- 4/0		
6- 13/1		
7- 26/0		
8- 3/0		
9- 9/4		
10- 11/3		
11- 19/0		
12- 9/0		
13- 1/0		
14- 7/3	1-	12/0
15- 3/0	2-	4/0
16- 5/0	3-	10/1
17- 16/1	4-	5/0
18- 8/0	5-	12/0
19- 10/7	6-	6/0
20- 6/0	7-	16/0
21- 4/0	8-	22/0
22- 8/0	9-	13/0
23- 10/0	10-	10/0
24- 3/0	11-	18/0
25- 25/0	12-	15/0
26- 16/0	13-	4/2
27- 21/0	14-	3/0
28- 10/0	15-	31/2
29-11/0	16-	24/19
30-23/5	17-	5/0
31-3/0	18-	21/4
32-5/0	19-	15/1
33-14/0	20-	0/0
34-31/1	21-	20/0
35-6/0	22-	17/2
36-13/0	23-	11/0
37-13/0	24-	19/0
38-22/0	25-	11/0
39-20/0	26-	14/0
40-17/2	27-	11/2
41-15/0	28-	14/6
42-12/0		
43-22/0		
44-6/0		
45-24/4		
46- 16/0		
47- 13/4		
48- 7/0		
49- 18/0		
50- 25/3		
51- 14/0		
52- 12/0		
53- 19/0		
54- 11/0		

55- 21/0
56- 15/7
57- 0/0
58- 7/0
59- 14/7
60- 3/0
61- 13/0
62- 8/0
63- 13/0
64- 14/11
65- 11/0
66- 15/1
67- 24/0
68- 12/1
69- 24/0
70- 23/0
71- 15/0
72- 14/2
73- 17/0
74- 39/5
75- 5/0
76- 8/0
77- 21/0
78- 20/0
79- 13/0
80- 16/2
81- 12/2
82- 15/10
83- 15/3
84- 15/0
85- 11/4
86- 12/0
87- 16/0
88- 26/0
89- 18/0
90- 20/0
91- 19/0
92- 11/5
93- 5/0
94- 15/4
95- 18/0
96- 13/0
97- 34/0
98- 21/2
99- 14/6
100- 8/0
101- 11/0
102- 17/4
103- 16/0
104- 15/5
105- 24/0
106- 17/0
107- 12/0
108- 11/0
109- 11/0
110- 14/0
111- 13/4
112- 12/1
113- 11/1
114- 13/0
115- 11/0
116- 18/0
117- 13/0
118- 24/7
119- 12/0
120- 17/1
121- 14/1
122- 14/0
123- 10/2
124- 10/0

The number of cases with lymph nodes harvested ≥ 12 was significantly higher (P value of <0.2) in the laparoscopic procedure (61.1% of cases) compared to the open procedure (57.1% of cases) respectively (Table 3).

Table 3: No of Lymph Nodes ≥ 12 in Laparoscopic vs. Open Cohort

Laparoscopic cohort with number of cases =/> 12 lymphnodes	Open procedure cohort with number of cases =/> 12 lymphnodes
82/124	16/28
Percentage of lymphnodes yielding	Percentage of lymphnode yielding
66.1%	57.1%

The same Number of cases were reported with positive lymph nodes in both technique with very marginal difference of 0.1% more in laparoscopic procedure (table4)

Table 4: No of Positive Lymph Nodes Yield in Both Cohort

Laparoscopic procedure	Open procedure
40/124	9/28
Percentage	Percentage
32.2%	32.1%

The ratio of positive lymph node when the yield >12 was higher in laparoscopy 0.8 comparing with open 0.6. When the yield < 12 the ratio of positive lymph node almost comparable with 0.2 in laparoscopy and 0.3 in open technique (table5)

Table 5: Ratio of Positive Lymph Node Compared in >/< 12 Nodes Yielded

Laparoscopic procedure: No of patients with positive lymohnode and =/> 12 lymphnodes yielded	Open procedure: No of patients with positive lymohnode and =/> 12 lymphnodes yielded
32/40	6/9
No of patients with positive lymohnode and < 12 lymphnodes yielded	No of patients with positive lymohnode and <12 lymphnodes yielded
8/40	3/9

5. Discussion

The study showed laparoscopy is standard of care in UHL with minor cases underwent open procedures for CRC. The stage of CRC and state of elective vs emergency were not involved in the study, this pitfalls might explain indication of open procedures in certain cases but still each yielded lymph nodes plotted correctly from total number of each Cohort.

Laparoscopic technique in addition to it is multiple advantages proved in most of published studies in literature review; it also oncologically have better out come as this study showed with 66.1% of cases underwent laparoscopic procedure =/> 12 lymph node while only 57.1% in open cohort . Still the study showed no difference between the two techniques in yielding positive lymph nodes.

Positivity of harvested lymph node have great impact in management of CRC patients and determined their need of neoadjuvant chemotherapy in addition to it is major effect in 5 year survival rate with it is reduction to 40% compared to > 70% in negative lymph nodes patient as shown in Trepanier M, et al.

From table2 the Data manifested the highest number of lymph nodes harvested in both group which is 39 in laparoscopic cohort while the highest number in open cohort is 31 lymph nodes , this single Data result more supporting laparoscopy as effective oncological procedure when compared with open technique.

The total number of positive lymph nodes increased significantly when total yielded nodes increased as shown in table 5 using the number of 12; again laparoscopy showed upper hand over open procedure in yielding positive lymph node in table 5.

The study lack specification of location of CRC (Rt hemicolectomy , anterior resection , TME … extra), prior CRC staging of samples before surgery, elective vs emergency resection, and factor of Neoadjuvant chemotherapy.

Open procedures CRC cohort have small sample only 28 cases compared to 124 cases in laparoscopic cohort which might lack comparability between the two samples in the study but quite difficult to find sufficient open procedures Data from 2012 forward as laparoscopy was standard of care in the time period of study in most of centres.

The study revealed colorectal surgeons will have no sufficient numbers of open CRC procedures to keep sufficient numbers for hand on practice and experience since open oncological procedures occasionally indicated as primary care in certain patients.

The pitfall of cost needed by laparoscopy is actually compensated by shorter hospital stay and less morbidity, There are many major randomized controlled trials that compared laparoscopic versus open surgery for colon cancer: the Milsom trial, Barcelona trial, COST (the U.S.) trial, COLOR (European) trial, and CLASICC (U.K.) trial.[10,11,12,13,14] All of these studies reported similar short-term-outcome advantages associated with laparoscopic surgery. Laparoscopic colon surgery was associated with a significantly lower intensity of pain,

less narcotic use and estimated blood loss, shorter postoperative ileus and length of stay. The Barcelona trial was the only one of these trials to show a significant decrease in postoperative morbidity rate after laparoscopy (11%) compared with open (29%, $p < 0.001$).[4] Another consistent finding among these studies was significantly longer operative time for the laparoscopic surgery group. Postoperative recovery of pulmonary function has been shown to be quicker after laparoscopic colectomy in several studies. Milsom et al[14] in a randomized trial showed that pulmonary function as measured by the forced expiratory volume (FEV_1) and forced vital capacity (FVC) improved significantly faster in the laparoscopic than in the open group (3 versus 6 days).

None of the randomized trials showed significant difference in anastomotic leakage rates or wound infection rates between the laparoscopic and open groups. [10 - 14].

The study support laparoscopic CRC procedure as it have better oncological outcome when compared to open procedure using lymph node yield as single oncological factor, certain cases like; T4 colorectal cancer, locally advanced tumour, medical conditions and obstructed CRC might need open procedure. Fall of open cases in highly equipped centres might necessitate evolving of new surgeons dealing only with indicated open procedures.

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